Z. ZHANG,* W. ZHANG, J. LI, Q. LIU, T. LIU, G. ZHANG* (HENAN NORMAL UNIVERSITY, XINXIANG, P. R. OF CHINA)

Synthesis of Multisubstituted Pyrroles from Doubly Activated Cyclopropanes Using an Iron-Mediated Oxidation Domino Reaction


Iron-Mediated Synthesis of Pyrroles from Cyclopropanes

Significance: The synthesis of highly substituted pyrroles 3 from cyclopropanes 1 and amines 2 via an iron-mediated sequential ring opening–cyclization–dehydrogenation reaction is reported. The conditions were optimized using different solvents, reaction times, and iron catalysts. The scope was studied and cyclopropanes 1 bearing methyl and aryl substituents at R1 were tested with the latter giving better yields. EWG- and EDG-substituted aryl amines as well as R2 = OEt were well tolerated. Also, a methyl group in the cyclopropane (R4 = Me) was suitable, furnishing 1,2,3,5-substituted pyrrole 3 in good yield. A series of aromatic and aliphatic amines were screened as well: aliphatic amines furnished pyrroles 3 in low yields, while aromatic amines gave better results, although the yields decrease according to the position of the phenyl substituent. A reaction mechanism involving a radical process was suggested based on radical trapping experiments.

Comment: Cyclopropane derivatives can be used as precursors to synthesize a variety of useful heterocyclic motifs (C. A. Carson, M. A. Kerr Chem. Soc. Rev. 2009, 38, 3051; J. R. Green, V. Snieckus Synlett 2014, 25, 2258). The present work reports an efficient synthesis of tri- and tetra-substituted pyrroles in moderate to good yields from readily available cyclopropanes and amines. The reaction shows a broad substrate scope; both EWG and EDG-substituted aryl amines were well tolerated. Also, a methyl group in the cyclopropane (R4 = Me) was suitable, furnishing pyrroles 3 in comparable yields. While anilines with different patterns of substitution furnished 3 in good yields, a large excess of amine was required when benzylamines were used. The readily available cyclopropanes can be easily prepared in high yields by the reaction of a dicarbonyl compound with 1,2-dibromoethane (Z. Zhang et al. Angew. Chem. Int. Ed. 2007, 46, 1726).